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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/574,697	04/05/2006	Jiro Kishimoto	23757-009US1 / SSD-P848-U	3729
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FISH & RICHARDSON PC P.O. BOX 1022 MINNEAPOLIS, MN 55440-1022			KOSAR, AARON J	
			ART UNIT	PAPER NUMBER
			1651	
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

PATDOCTC@fr.com

Office Action Summary	Application No. 10/574,697	Applicant(s) KISHIMOTO ET AL.	
	Examiner AARON J. KOSAR	Art Unit 1651	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 7/9/2008.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-36 is/are pending in the application.
- 4a) Of the above claim(s) 1-10 and 17-36 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 11-16 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
1. ☒ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date <u>1/8/08; 7/9/08</u> . | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Response to Amendment

Applicant's amendment and argument filed July 9, 2008 in response to the non-final rejection are acknowledged and have been fully considered. Applicant has amended the claims 11-16. Claims 1-36 are pending of which claims 1-10 and 17-36 are withdrawn claims. **Claims 11-16** are pending and have been examined on the merits. . Any rejection and/or objection not specifically addressed is herein withdrawn.

Claim Rejections - 35 USC § 112, 1st ¶

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Response to Arguments

Applicant has canceled the term "hair follicle" and has argued Chuong with respect to this term. Applicant has also argued that the claims may have inoperative embodiments. Applicant's arguments have been fully considered, however, respectfully they are found to be not persuasive, for the reasons of record and as presented below.

With respect to the Applicant's arguments over the term "hair follicle" the cancellation of the term has rendered Applicant's arguments and the rejections *to the extent of said term* moot.

With respect to Applicant's arguments that inoperative embodiments do not render the claims indefinite, Applicant's arguments are respectfully found to be not persuasive, because the instant claims are directed towards an immeasurable number of organismal or mammalian cell combinations having *a priori* indeterminate operability, wherein only a limited number of

species of cell combinations (e.g. the disclosed human, mouse, and/or rat cell combinations) are provided as having the desired function. Additionally, among said limited number of disclosed species, said species are not representative of the genus, by Chuong's teaching that the combination of human:human is inoperative in the desired/disclosed manner. Thus for the reasons of record and those provided herein *and* considering the diversity of the genus and the unpredictability even among the limited disclosed species combinations, one would be burdened with undue experimentation to make and/or use the invention commensurate in scope to the extent instantly claimed.

Claims 11-16 are/remain rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for select species of mammalian cell compositions, does not reasonably provide enablement for all compositions. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

The factors to be considered in determining whether a disclosure meets the enablement requirements of 35 U.S.C. 112, first paragraph, have been described in In re Wands, 858 F.2d 731, 8 USPQ2d 1400 (Fed. Cir., 1988). The court in Wands states, "Enablement is not precluded by the necessity for some experimentation, such as routine screening. However, experimentation needed to practice the invention must not be undue experimentation. The key word is 'undue', not 'experimentation'" (Wands, 8 USPQ2d 1404). Clearly, enablement of a claimed invention cannot be predicated on the basis of quantity of experimentation required to make or use the invention. "Whether undue experimentation is needed is not a single, simple factual determination, but rather is a conclusion reached by weighing many factual considerations" (Wands, 8 USPQ2d 1404). Among these factors are: (1) the nature of the invention; (2) the breadth of the claims; (3) the state of the prior art; (4) the predictability or unpredictability of the art; (5) the relative skill of those in the art; (6) the amount of direction or guidance presented; (7) the presence or absence of working examples; and (8) the quantity of experimentation necessary.

While all of these factors are considered, a sufficient amount for a *prima facie* case is discussed below.

(1) The nature of the invention and (2) the breadth of the claims:

The claims are generally drawn to a hair-growth/skin-regenerating composition using cells from any organismal source (or combination of organisms).

The specification and examples teach cellular structures which produce a partial approximation of the behavior of a hair follicle-like structure with species of mammalian cell combinations. The specification teaches, for example, the specific cell combinations including the skin dermal papilla cell:epidermal cell heterogeneous combinations of human:mouse and of mouse:rat *and* the homogeneous combination of mouse:mouse.

Thus, the claims taken together with the specification imply a broader breadth than what is supported by the specification.

(3) The state of the prior art and (4) the predictability or unpredictability of the art:

The state of the art is such that follicle/hair regeneration is unresolved and unpredictable.

INAMATSU (US 5,851,831, of record) teaches that cell proliferation, differentiation of dermal-epidermal cells in contact, and maintenance of dermal papilla (DP) function in epidermal-dermal papilla compositions is known. Inamatsu teaches that “culturing dermal papilla cells with at least either of mammalian epidermal cells from the sole or other portions of a mammal, and the conditioned medium thereof, in order to permit long stable subculture of dermal papilla cells while keeping the original function thereof intact.” (Abstract). Inamatsu also teaches that “it has been conventionally known that..interactions between the follicle epidermis and the underlying papillae result in the differentiation and proliferation of hair matrix cells, thereby causing the hair shaft (so-called hair body) to grow.”(column 1, ¶1). This teaches to one of skill that the contacting of DP and epithelial cells for the purpose of culture stability and hair-shaft growth.

STENN (X:PTO-892)) teaches that “hair follicles are not formed nor do they function, normally in the absence of a sebaceous gland” (page 1, ¶1). This teaches to one of skill that the

instantly claimed composition, absent an associated sebaceous gland and organization of cells functioning in the manner as a hair follicle, is not itself a hair follicle *per se*.

Furthermore, CHUONG (W:PTO-892), also teaches that the complex organ of a follicle is greater than a keratinaceous shaft and that the organ includes an array of spatially arranged specialized tissues and periodicity of hair cycles (pages 2098-2099; table 1). Chuong, in reference to the composition of EHAMA (V:PTO-892), also teaches that the myriad of sources of epidermal cells may provide “different competences” (page 2100), and **“homospecific human cells did not work”** (page 2098, emphasis added). Also, Chuong teaches that the putative follicle reported by Ehama (V) is not a true follicle but an approximation of a keratin plug-growing mimic thereof. Chuong summarizes these differences/deficiencies by stating:

The reconstituted hair follicles using homospecific mouse or rat cells clearly generate normal-appearing hairs. Heterospecific mouse–rat combinations are also good. Homospecific human cells did not work in Ehama and colleagues' experiments, but human–mouse combinations gave results that formed the basis of the current report. The authors reported that epidermal invaginations from the reformed epidermis occur. A cluster of dermal condensation cells was located adjacent to the follicle but was not engulfed by the follicle base. It was alkaline-phosphatase-positive, but versican-negative. Whether it can be considered a bona fide DP is debatable, but the structure was distinct from the surrounding cells and appeared closer to DP than other tissues. Proliferating cells were distributed in the basal epidermal layer but not localized to the matrix region. There were no K15-positive bulge cells, nor did they demonstrate the presence of stem cells by any other methods (Cotsarelis, 2006). The topologic arrangement of stem, TA, and differentiated cells seen in normal hair follicles did not appear to form. Follicular epidermal cells were layered, but the distinct differentiation of medullar, cortex, and inner and outer root sheath was unclear. The poorly formed hair shaft–like structure is better described as a keratin plug than as a hair shaft. None of the structures had associated sebaceous glands. As for biochemical differentiation, hair keratin Hb1 and AE 13 were weakly positive, and transglutaminase 1 was not found. The authors did not demonstrate cycling behavior of the hair follicle–like structures either, which is why the newly formed structures can only be called “hair follicle–like.” Although they did not achieve the engineering of a “real” human hair follicle, the article demonstrates work in progress toward this goal. ((emphasis added) Chuong, page 2098, ¶ 2 and portion spanning page 2099)

The art of Ehama shows the differentiation of cells and select activities of the product

composition(s); however, as argued by Chuong (*supra*), the composition does not replicate a follicle *per se*, is a “work in progress” towards a follicle-regenerating composition, and also unpredictable with respect to the mammalian cell combinations employed.

The art of Chuong and Ehama teach one of skill that in the art, selection of cell combinations is unpredictable except to the extent of those combinations demonstrated as functioning in the desired/disclosed manner.

Since the determination of an art-recognized regenerated follicle appears absent in the prior art and since compositions approximating such a composition, to the extent claimed, are unresolved with respect to the myriad of cell:cell combinations (in)capable of functioning in the requisite manner, then means for producing a composition useful in hair-/skin-regenerating is highly unpredictable, except to the extent of the instantly disclosed species of cell:cell combinations capable of functioning in the claimed/disclosed manner.

(5) The relative skill of those in the art:

The relative skill of those in the art is high; however, with respect to producing a composition which is capable of functioning in the claimed/disclosed manner is beyond the purview of the skilled artisan.

(6) The amount of direction or guidance presented and (7) the presence or absence of working examples:

The specification has provided examples of cell compositions, including those from human/murine, mouse/mouse, mouse/rat, etc; however, the specification does not provide human/human compositions, *or* other cells (mammalian or non-mammalian), *or* combinations representative of all compositions embraced by the genus of compositions claimed. In view of

the limited number of working examples and guidance presented *and* the unpredictability of the species of the combination of human:human (homospecific) cells as argued by Chuong (*supra*) the species presented cannot be considered representative of the genera claimed (*all* mammalian cells, cells, tissue, etc).

(8) The quantity of experimentation necessary:

Considering the state of the art as discussed by Chuong and Ehama and the high unpredictability and the lack of guidance provided in the specification, one of ordinary skill in the art would be burdened with undue experimentation to make and use the invention.

It is the Examiner's position that one skilled in the art could not practice the invention commensurate in scope with these claims without undue experimentation.

Claim Rejections - 35 USC § 112, 2nd ¶

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Response to arguments

Applicant has argued that "about" does not render the claims indefinite. Respectfully, Applicant's arguments are not found to be persuasive, because, for the reasons of record, "about" is open language and in combination with the claimed closed range provides a combination of both a closed and open language which is not further limiting of the narrower closed "from/to" range, especially in the absence of definition to which a composition may/may not qualify as a composition "about" the extent claimed.

Claim 12 remains rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A broad range or limitation together with a narrow range or limitation that falls within the broad range or limitation (in the same claim) is considered indefinite, since the resulting claim does not clearly set forth the metes and bounds of the patent protection desired. See MPEP § 2173.05(c). Note the explanation given by the Board of Patent Appeals and Interferences in *Ex parte Wu*, 10 USPQ2d 2031, 2033 (Bd. Pat. App. & Inter. 1989), as to where broad language is followed by "such as" and then narrow language. The Board stated that this can render a claim indefinite by raising a question or doubt as to whether the feature introduced by such language is (a) merely exemplary of the remainder of the claim, and therefore not required, or (b) a required feature of the claims. Note also, for example, the decisions of *Ex parte Steigewald*, 131 USPQ 74 (Bd. App. 1961); *Ex parte Hall*, 83 USPQ 38 (Bd. App. 1948); and *Ex parte Hasche*, 86 USPQ 481 (Bd. App. 1949). In the present instance, claim 12 recites the broad recitation "about 1:1", and since the term "about" is a term of degree (a dynamic term, analogous in structure to the term "comprising") which is not further defined by the specification, "about 1:1" may reasonably be interpreted to include a broad range of dermal papilla cell:epidermal cell ratios; however, the claim also recites the narrower range of "from 1:10 to 10:1" which is a narrower statement (a static term, analogous in structure to the term "consisting") of range/limitation. As noted supra, by the claim 12 depending upon the ranges of both about 1:1 and/or from 1:10 to 10:1, it is unclear if about 1:1 is exemplified by the static range (from 1:10 to 10:1) or if the static range is required by the claim. One of skill would not be apprised as to the metes and bounds of the claims, rendering the claims indefinite.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to AARON J. KOSAR whose telephone number is (571)270-3054. The examiner can normally be reached on Monday-Thursday, 7:30AM-5:00PM, ALT. Friday,EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mike Wityshyn can be reached on (571) 272-0926. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Application/Control Number:
10/574,697
Art Unit: 1651

Page 10

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Aaron Kosar
Examiner, Art Unit 1651

/Sandra Saucier/
Primary Examiner, Art Unit 1651